Baldwin, et al. generically describe a myriad of Class III potassium channel blocking antiarrythmic agents (col. 2 lines 59-67 through col. 6, line 63), specifically list 40 preferred species (30 of which are sulfur-containing compounds) by name (col. 10, lines 24-67 through col. 12, line 9) and exemplify more than 566 such agents (col. 19, line 48 through col. 212, line 23). There is no further description of preferred agents. Nothing in Baldwin et al. describes or suggests using any of these agents in an assay that uses a membrane, containing the rapid component of the delayed rectifier current (IK_r) channel protein derived from a cell line capable of being stably transfected with ERG (ether-a-go-go-related gene) and expressing the IK_r channel protein, to characterize the activity of a compound as an IK_r channel blocker. Baldwin, et al. makes no mention at all of this channel protein, and does not provide any teaching that would lead a person having ordinary skill in the art to make [^{35}S]-radiolabeled (+)-N-[1'-(6-cyano-1,2,3,4-tetrahydro-2(R)-naphthalenyl)-3,4-dihydro-4(R)-hydoxyspiro[2H-1-benzopyran-2,4'-piperidin]-6-yl]-methanesulfonamide and use this radioligand compound in the claimed method.

Baldwin, et al., in combination with each of Chadwick, et al., Fiset, et al., Geonzon, et al., or Duff, et al., also fail to make the claimed method of using a membrane containing the IK_r channel protein and [^{35}S]-radiolabeled (+)-N-[1'-(6-cyano-1,2,3,4-tetrahydro-2(R)-naphthalenyl)-3,4-dihydro-4(R)-hydoxyspiro[2H-1-benzopyran-2,4'-piperidin]-6-yl]-methanesulfonamide to characterize the activity of a compound as an IK_r channel blocker obvious to a person having ordinary skill in the art. Chadwick, et al. identified [^{3}H]-dofetilide as a radioligand that could be used for the rapidly activating delayed rectifier potassium channel of the heart by demonstrating binding to high affinity sites on guinea pig cardiac myocytes. Fiset, et al. characterized [^{3}H]-dofetilide binding on guinea pig myocytes, neonatal mouse ventricular homogenate and untransfected CHO cells. Geonzon, et al. characterized binding of [^{3}H]-dofetilide to human leukocytes obtained from whole blood samples. Duff, et al. characterized binding of [^{3}H]-dofetilide to guinea pig (which expresses IK_r) and rat (which does not express IK_r) cardiac myocytes.

Applicants maintain that a person having ordinary skill in the art would not find the claimed assay obvious in view of Baldwin, et al. in combination with each of Chadwick, et al., Fiset, et al., Geonzon, et al., or Duff, et al. None of these references teaches or suggests using [^{35}S]-radiolabeled (+)-N-[1'-(6-cyano-1,2,3,4-tetrahydro-2(R)-naphthalenyl)-3,4-dihydro-4(R)-hydoxyspiro[2H-1-benzopyran-2,4'-piperidin]-6-yl]-

methanesulfonamide in an assay, and none of the references teaches or suggests using a membrane, containing IK_r channel protein derived from a cell line capable of being stably transfected with ERG and expressing the IK_r channel protein, in an assay. Certainly, the references, alone or in combination, do not teach or suggest a method of using a membrane containing the IK_r channel protein and [^{35}S]-radiolabeled (+)-N-[1'-(6-cyano-1,2,3,4-tetrahydro-2(R)-naphthalenyl)-3,4-dihydro-4(R)-hydoxyspiro[2H-1-benzopyran-2,4'-piperidin]-6-yl]-methanesulfonamide to characterize the activity of a compound as an IK_r channel blocker.

Finally, Dean, et al. merely discuss radiolabeling considerations using ^{35}S, and do not provide any additional teaching or suggestion for using a membrane containing IK_r channel protein derived from a cell line capable of being stably transfected with ERG and expressing the IK_r channel protein and [^{35}S]-radiolabeled (+)-N-[1'-(6-cyano-1,2,3,4-tetrahydro-2(R)-naphthalenyl)-3,4-dihydro-4(R)-hydoxyspiro[2H-1-benzopyran-2,4'-piperidin]-6-yl]-methanesulfonamide to characterize the activity of a compound as an IK_r channel blocker.

Applicants respectfully maintain that none of the references cited and applied by the Examiner teaches or suggests [^{35}S]-radiolabeled (+)-N-[1'-(6-cyano-1,2,3,4-tetrahydro-2(R)-naphthalenyl)-3,4-dihydro-4(R)-hydoxyspiro[2H-1-benzopyran-2,4'-piperidin]-6-yl]-methanesulfonamide, none of the references cited and applied by the Examiner teaches or suggests membranes containing IK_r channel protein derived from a cell line capable of being stably transfected with ERG and expressing the IK_r channel protein, and the references, in combination, do not suggest the presently claimed assay using this radiolabeled compound and described membranes, to characterize the activity of a compound as an IK_r channel blocker. Applicants believe these references do not make the claimed invention obvious to a person having ordinary skill I the art.

Respectfully submitted,

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Richard S. Parr
Attorney for Applicants
MERCK & CO., Inc.
P.O. Box 2000
Rahway, NJ 07065-0907
Tel.: (732) 594-4958